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Labor neuraxial analgesia and breastfeeding: an updated systematic review

Heesen, Philip ; Halpern, Stephen H ; Beilin, Yaakov ; Mauri, Paola A ; Eidelman, Leonid A ; Heesen, Michael ; Orbach-Zinger, Sharon

Abstract: Introduction: There have been numerous reports studying the effect of neuraxial analgesia on breastfeeding success, but the results are inconsistent. Methods: We performed a literature search in various databases for studies comparing neuraxial analgesia to non-neuraxial or no analgesia. Outcomes were the percentage of women breastfeeding fully or mixed with formula. Where possible, nulliparous parturients were analyzed separately. We conducted an analysis excluding studies of serious and critical risk of bias. Odds ratios and 95% confidence intervals were calculated. Results: We included 15 studies (13 observational studies, 1 secondary analysis of a randomized controlled trial, 1 case-control study) with 16,112 participants. Overall, there were 6 studies that found no difference between groups, 6 studies that showed a significantly lower incidence of breastfeeding in the neuraxial group and 3 studies finding mixed results (at some time-points statistically significant and at some time-point statistically non-significant results). In nulliparous only studies, 2 found no difference between study groups, 1 found a lower breastfeeding rate in the neuraxial group and 3 studies showed mixed results. Excluding studies with a serious and critical risk of bias, 1 study found no difference between study groups, 3 studies found a decrease of breastfeeding rates in the neuraxial group, and 1 study showed mixed results. Discussion: In our review we found a high disparity in results. One reason is probably the high potential of confounding (immediate skin to skin placement, maternity leave etc.). Education programs and breastfeeding support are likely more important in determining long term breastfeeding success.

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Labor neuraxial analgesia and breastfeeding: An updated systematic review

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ABSTRACT

Introduction: There have been numerous reports studying the effect of neuraxial analgesia on breastfeeding success, but the results are inconsistent.

Methods: We performed a literature search in various databases for studies comparing neuraxial analgesia to non-neuraxial or no analgesia. Outcomes were the percentage of women breastfeeding fully or mixed with formula. Where possible, nulliparous parturients were analyzed separately. We conducted an analysis excluding studies of serious and critical risk of bias. Odds ratios and 95% confidence intervals were calculated.

Results: We included 15 studies (13 observational studies, 1 secondary analysis of a randomized controlled trial, 1 case-control study) with 16,112 participants. Overall, there were 6 studies that found no difference between groups, 6 studies that showed a significantly lower incidence of breastfeeding in the neuraxial group and 3 studies finding mixed results (at some time-points statistically significant and at some time-point statistically non-significant results). In nulliparous only studies, 2 found no difference between study groups, 1 found a lower breastfeeding rate in the neuraxial group and 3 studies showed mixed results. Excluding studies with a serious and critical risk of bias, 1 study found no difference between study groups, 3 studies found a decrease of breastfeeding rates in the neuraxial group, and 1 study showed mixed results.

Discussion: In our review we found a high disparity in results. One reason is probably the high potential of confounding (immediate skin to skin placement, maternity leave etc.). Education programs and breastfeeding support are likely more important in determining long term breastfeeding success.

1. Introduction

The World Health Organization advises initiating breastfeeding within the first hour of birth and continuing for at least six months. [1] Breast milk is considered the ideal food for the newborn, containing both nutrients and antibodies, thus protecting infants from diarrhea and pneumonia, the two main causes of child mortality worldwide. [1] Infants that were breastfed were found to have a lower chance of experiencing sudden infant death syndrome or suffering from respiratory infections, asthma, type I and II diabetes and leukemia. [2] Adults that were breastfed as infants have been shown to be less obese and have higher IQ scores. [3]

For the mother, breastfeeding has many advantages. Early breastfeeding leads to increased uterine contractions. [4] Breastfeeding has been shown to accelerate the return to the mother's pregestational weight and is associated with a decreased risk of developing postpartum depression. [5] Beneficial outcomes of breastfeeding for the mother are decreased chances of developing type II diabetes and both ovarian and breast cancer. [2]

Neuraxial analgesia (NA) provides safe and effective pain relief in labor. In the United States, 73% of all deliveries are done using NA. [6] However, some studies have shown that NA leads to a lower incidence of breastfeeding postpartum. [7,8] In a large prospective observational study, women who received NA had a reduced likelihood of

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breastfeeding when compared with their counterparts who had not received NA. [9] In contrast, two other studies found no association of NA on breastfeeding success at 6–8 weeks. [10,11]

Furthermore, there have been conflicting results of neuraxial labor analgesia on infant neurobehavior. However, it is unclear how initially decreased infant neurobehavioral scores, if at all occurs, would influence long-term breastfeeding.

In order to resolve this discrepancy, we set out to gather all available evidence by performing a systematic literature search of studies that looked at the association of NA versus non-NA or no analgesia on breastfeeding. Breastfeeding was defined as a binary variable (breastfeeding success yes/no) where exclusive or mixed breastfeeding was considered breastfeeding success. We performed a systematic review looking at the time interval from immediately after birth to 8 weeks postpartum.

2. Methods

Our study conforms with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. [12] We conducted a systematic literature search in the following databases: Medline, EPUB, embase.com (Embase plus Medline), Cochrane Central, Web of Science, Google scholar (until 27.09.2019). Details of the search strategy are given in the online supplement [ref]. Fig. 1 shows a flow chart of the literature search.

The articles found were then entered into Endnote X9 (Clarivate Analytics, Jersey) which was further used to avoid duplication. The bibliographies of the retrieved articles were also hand searched to identify additional references. Language restrictions were English, French, German, Hebrew. We only included full text articles. In addition, we contacted authors of retrieved manuscripts for additional data.

We used the following PICO format: P: women intending to undergo vaginal delivery and that had the intervention (I) of NA (either epidural analgesia (EA) or a combined spinal-epidural analgesia (CSE)). Our comparison (C) group included parturients having either non-neuraxial analgesia (neither CSE nor EA) or no analgesia at all. The primary outcome (O) was defined as breastfeeding success (including a combination of breastfeeding and formula) immediately after birth to 8 weeks postpartum.

Breastfeeding success was defined using one of four methods as defined by the authors of the manuscripts included:

1. Dichotomous outcome breastfeeding (yes/no).
2. Infant Breastfeeding Assessment Tool (IBFAT) with a score ≥ 10 as an indication of breastfeeding. [13]
3. LATCH score with a LATCH score of ≥ 7 out of 10 and 2/2 on the latch component being considered breastfeeding. [14]
4. LATCH score only looking at the L, A and C-components with a score of 6/6 considered breastfeeding. [15]

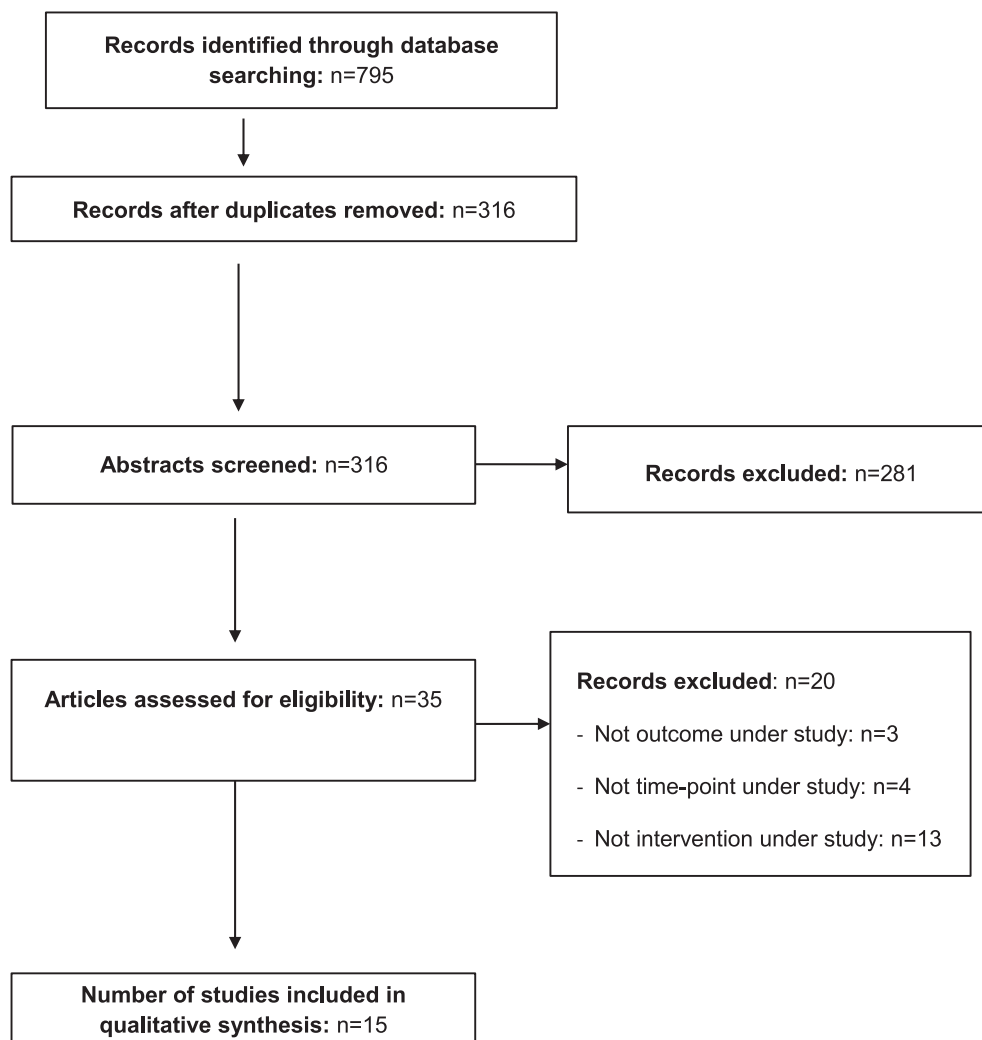


Fig. 1. Flow chart of the literature search.

Table 1
Study data. Results are presented as Odds Ratio (OR) and 95% Confidence intervals.

Study/Year/ Country	Type of Study	Outcome	Participants	Neuraxial	Control Group	Inclusion	Exclusion	Results
Armani/2013/ Italy [18]	Retrospective case-control	Breastfeeding at discharge (yes/no)	1963 (287 Neuraxial 1676 Control)	EA Levobupivacaine or ropivacaine	No analgesia (No details)	n.d.	CS, multiple pregnancies, < 34 weeks of gestation	OR 1.09 (0.46; 2.60)
Baumgardner/2002/USA [24]	Prospective observational	Two successful breastfeeding by 24 h (i.e. LATCH $\geq 7/10$ + latch 2/2)	231 (115 Neuraxial 116 Control)	EA (No details)	Non-EA (No details)	healthy full term neonate, delivered vaginally, mothers aged 16 to 41 with no complication	n.d.	OR 0.53 (0.29; 0.99)
Chang/2005/ Canada [15]	Prospective cohort	Breastfeeding at 8 to 12 h (LAC score of the LATCH = 6) and at 4 weeks (yes/no)	115 (52 Neuraxial 63 Control)	EA Bupivacaine or Ropivacaine Fentanyl ($n = 112$) Epinephrine ($n = 16$)	No analgesic medication (No details)	> 18 years, uncomplicated pregnancy + labor + vaginal delivery, healthy term and breastfeeding infant	n.d.	At 8–12 h: OR 0.65 (0.31; 1.36) At 4 weeks: OR 1.48 (0.54; 4.08) At 3 days: OR 1.18 (0.38; 3.63)
Ding/2014/China [10]	Prospective cohort	Breastfeeding at 3 days and at 6 weeks (yes/no)	214 (107 Neuraxial 107 Control)	EA or CSE Ropivacaine Sufentamil	No analgesic medication (No details)	consecutive nulliparas with term singleton cephalic pregnancy who were admitted to the delivery room and preparing to deliver vaginally during daytime working hours	history of psychiatric disease, obesity, EA contraindications	At 6 weeks: OR 2.39 (1.36; 4.19) At 3 days: OR 0.24 (0.10; 0.57) At 4 weeks: OR 0.59 (0.44; 0.80)
Dozier/2013/ USA [31]	Observational study with one prospective and one retrospective part	Breastfeeding cessation at 3 days and at 4 weeks	727 (437 Neuraxial 290 Control)	EA (No details)	Non-EA (No details)	English speaking, ≥ 18 years old, singleton term, low risk pregnancy, vaginal delivery	n.d.	aOR 1.26 (1.10; 1.44) OR 0.50 (0.17; 1.44)
Gizzo/2012/Italy [32]	Prospective observational	Correct sucking within the first 2 h postpartum (yes/no)	128 (64 Neuraxial 64 Control)	EA: Ropivacaine Fentanyl	No analgesic medication (No details)	primipara, 38–42 weeks of gestation, spontaneous or induced labor, neonatal birth weight 2500 to 4300 g, Apgar 1 > 7, Apgar 5 > 8	n.d.	OR 0.63 (0.46; 0.88)
Henderson/2003/ Australia [7]	Prospective observational	Breastfeeding at 2 months (yes/no)	663 (364 Neuraxial 299 Control)	CSE Bupivacaine Fentanyl	Non-CSE meperidine, nitrous oxide (Entonox [®]) or no analgesia	nullipara, singleton fetus, planned vaginal	< 37 weeks, contraindication to NA, refusal to participate	OR 0.46 (0.35; 0.60)
Herrera-Gomez/2015/Spain [22]	Retrospective cohort	Breastfeeding onset within first 2 h (yes/no)	2399 (551 Neuraxial 1848 Control)	EA: Ropivacaine or bupivacaine Fentanyl	Non-EA (No details)	> 37 weeks of gestation	induced labor, elective CS, pregnancy risk-factor (preexisting medical diseases or pregnancy/labor complication)	aOR 0.76 (0.64; 0.93) At 3 h: OR 0.75 (0.32; 1.76)
Mahmoodi/2019/ Iran [23]	Prospective cohort	Breastfeeding success at 3 h, at 24 h and at 4 weeks (yes/no)	383 (142 Neuraxial 241 Control); 4 weeks: 235 (86 Neuraxial 149 Control)	EA (No details)	Non-EA (No details)	vaginal birth, Iranian national, no infant abnormality	n.d.	at 24 h: OR 0.78 (0.17; 3.55) at 4 weeks: OR 0.86 (0.14; 5.27)

(continued on next page)

Table 1 (continued)

Study/Year/ Country	Type of Study	Outcome	Participants	Neuraxial	Control Group	Inclusion	Exclusion	Results
Mahomed/2019/ Australia [20]	Prospective cohort	Breastfeeding at discharge and at 6 weeks (yes/no)	304 (107 Neuraxial 197 Control)	EA Fentanyl	Non-EA subcutaneous morphine or no analgesia	multipara, intent to breastfeed, ≥ 37 weeks of gestation, understanding of English language	n.d.	At discharge: OR 0.44 (0.27; 0.71) at 6 weeks: OR 1.45 (0.87; 2.40)
Mauri/2014/Italy [19]	Prospective observational	Breastfeeding at 24 h and at 20 days (yes/no)	366 (209 Neuraxial 157 Control)	EA Ropivacaine or Levobupivacaine Sufentanil	Non pharmacologic or non- EA (No details)	healthy neonate, vaginal, 38 to 41 weeks of gestation, intention to breastfeed	< 18 years old, BMI < 18 or > 25, PPH with blood loss > 500 mL	aOR 0.75 (0.41; 1.38) At 24 h: OR 0.36 (0.13; 0.98)
Orbach-Zinger/ 2018/Israel [9]	Prospective observational cohort	Breastfeeding at 3 days and at 6 weeks (yes/no)	1204 (806 Neuraxial 398 Control)	EA Bupivacaine Fentanyl	Non pharmacologic (No details)	singleton vaginal delivery ≥ 37 weeks	< 18 years, contraindication for EA, no knowledge of Hebrew, baby in NICU, no intention to breastfeed	At 20 days: OR 0.72 (0.26; 1.98) At 3 days: OR 0.45 (0.27; 0.76)
Werzl/2019/Italy [8]	Community-based cohort study	Breastfeeding at discharge (yes/no)	3183 (637 Neuraxial 2546 Control)	CSE or EA Ropivacaine Sufentanil	Non-EA (No details)	vaginal delivery, singleton cephalic newborn, intention to breastfeed	dead fetus, unmarried women	at 6 weeks: OR 0.57 (0.41; 0.78) OR 0.65 (0.55; 0.78)
Wilson/2010/ England [17]	Randomized controlled trial	Breastfeeding initiation up to 2 h and at 24–48 h (yes/no)	1392 (1041 Neuraxial 351 Control)	CSE or EA: Fentanyl (only some of the parturients)	meperidine, 50% nitrous oxide (Entonox [®]), transcutaneous electrical nerve stimulation or no analgesia	multipara	contraindication to NA	At 3 h: OR 1.02 (0.80; 1.30)
Zuppa/2014/ Italy [25]	Cohort retrospective	Breastfeeding at 48–72 h/discharge (yes/ no)	2840 (1223 Neuraxial 1617 Control)	EA Ropivacaine Sufentanil	No analgesic medication (No details)	≥ 37 weeks, vaginal and uncomplicated delivery	Apgar 1/5 < 7, high risk pregnancy	at 24–48 h: OR 1.17 (0.91; 1.50) OR 1.14 (0.40; 3.20)

EA- Epidural analgesia, CSE- Combined Spinal and Epidural analgesia, CS- Cesarean section, NA- Neuraxial analgesia, NICU- Neonatal Intensive Care Unit, PPH- Postpartum hemorrhage, BMI- Body Mass Index.
n.d.- not determined, OR- odds ratio, aOR- adjusted odds ratio.

The IBFAT tool allows for a maximum score of 12, with three points in each of the four categories that evaluate sucking-, feeding- and rooting- patterns as well as the time it took from placing the baby on the mother's breast to latch and suck.

The LATCH score assesses individual breastfeeding sessions and looks at the following components: L: latching, A: amount of audible swallows, T: mother's nipple type, C: mother's level of comfort, H: amount of help the mother needs to hold her infant to the breast.

The reporting quality of all of the observational studies considered eligible was assessed using the ROBINS-I tool. [16]

Two researchers (SOZ, PH) independently screened the articles retrieved from the literature search for eligibility and three researchers (SOZ, PH, SH) independently performed the quality assessment and extraction of data and then compared their extracted data and quality assessment. Disagreement was settled by discussion and then consensus was found or by assessment by a third investigator (SH, MH). These reviewers did not judge their own studies, but a third reviewer was involved (SH and PH for SOZ).

Originally, we planned to combine the results of the systematic review in a meta-analysis. However, we found that there was too much clinical and statistical heterogeneity in the results to justify reporting a pooled effect size. We therefore decided to present the results of the review qualitatively. We calculated odds ratios (OR) and corresponding 95% confidence intervals (CI).

3. Results

We have included 15 studies with 16,112 participants that fit our inclusion criteria. Fourteen studies were observational studies, one study was a secondary analysis of a randomized controlled trial and one study was a case-control study. [17,18] Study details are presented in Table 1, the risk of bias assessment of each study is presented in Table 2. We found 2 studies with a critical risk of bias, 8 studies with a serious risk of bias, 4 studies with a moderate risk of bias, and 1 study with a low risk of bias.

Results for mixed-parity cohorts are presented in Table 3 sorted by delivery to measurement time order. Breastfeeding rates for mixed-parity cohorts measured between 2 and 8 weeks postpartum are presented in Fig. 2.

Nulliparous parturients.

There were 6 studies with 3127 parturients that studied nulliparous patients exclusively.

Two studies measured breastfeeding at 24 h postpartum using a dichotomous outcome and found no significant difference between the NA and control group (OR 0.38 (95% CI, 0.10; 1.41) [19], OR 1.17 (95%CI, 0.91, 1.50)) [17].

Two studies measured breastfeeding at 3 days using a dichotomous outcome. One of these studies found a significant reduction of breastfeeding in the NA group (OR 0.21 (95%CI 0.05; 0.92)) [9], whereas

Table 2
Risk of Bias assessment.

Article	Baumgardner [24]	Mahomed [20]	Zuppa [25]	Wetzel [8]
- Bias due to confounding	Moderate	Low/Moderate	Moderate/Serious	Low
- Bias in selection of participants into the study	Moderate	Moderate	Moderate/Serious	Low
- Bias in classification of interventions	Serious	Low/Moderate	Moderate	Low/Moderate
- Bias due to deviations from intended interventions	Low/Moderate	Moderate	Moderate	Low/Moderate
- Bias due to missing data	Moderate	Moderate	Moderate	Low
- Bias in measurement of outcomes	Moderate/Serious	Serious/Critical	Moderate	Low/Moderate
- Bias in selection of the reported result	Moderate/Serious	Moderate	Moderate	Low
Overall	Serious	Serious	Serious	Moderate

Article	Ding [10]	Mahmoodi [23]	Dozier [31]	Herrare Gomez [22]	Chang [15]
- Bias due to confounding	Critical	Critical	Moderate/Serious	Serious	Moderate
- Bias in selection of participants into the study	Serious/Critical	Critical	Serious	Serious	Moderate
- Bias in classification of interventions	Moderate	Critical	Moderate/Serious	Serious	Serious
- Bias due to deviations from intended interventions	Moderate	Critical	Moderate	Serious	Low/Moderate
- Bias due to missing data	Critical	Critical	Serious	Moderate	Moderate
- Bias in measurement of outcomes	Critical	Critical	Moderate/Serious	Serious	Serious
- Bias in selection of the reported result	Moderate	Critical	Low/Moderate	Low/Moderate	Low/Moderate
Overall	Critical	Critical	Serious	Serious	Serious

Article	Henderson [7]	Orbach-Zinger [9]	Mauri [19]	Armani [18]
- Bias due to confounding	Moderate	Low	Low/Moderate	Serious
- Bias in selection of participants into the study	Moderate	Moderate	Moderate	Serious
- Bias in classification of interventions	Moderate	Low	Moderate	Moderate/Serious
- Bias due to deviations from intended interventions	Low	Low	Moderate	Moderate
- Bias due to missing data	Low	Low/Moderate	Serious	Moderate
- Bias in measurement of outcomes	Moderate	Low	NI	Serious
- Bias in selection of the reported result	Low	Low/Moderate	Low	Serious
Overall	Moderate	Moderate	Moderate	Serious

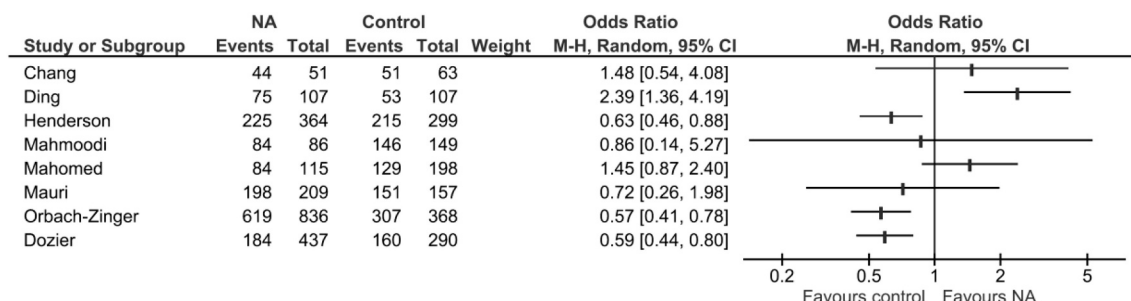
Article	Gizzo [32]	Wilson [17]
- Bias due to confounding	Serious	Low
- Bias in selection of participants into the study	Serious	Low
- Bias in classification of interventions	Moderate	Low
- Bias due to deviations from intended interventions	Moderate/serious	Low
- Bias due to missing data	Moderate	Low
- Bias in measurement of outcomes	Serious	Low
- Bias in selection of the reported result	Serious	Low
Overall	Serious	Low

Table 3

Results listed in a chronological order. Results are presented as Odds ratios (OR) and 95% Confidence Intervals.

Time-period	No significant difference between groups	Significantly lower rate of breastfeeding in the NA group	Significantly higher rate of breastfeeding in the NA group
2 h	2 OR 0.50 (0.17; 1.44) [32] OR 1.02 (0.80; 1.30) [17]	1 OR 0.46 (0.35; 0.60) [22] aOR 0.76 (0.64; 0.93) [22]	
3 h	1 OR 0.75 (0.32; 1.76) [23]		
8 to 12 h	1 OR 0.65 (0.31; 1.36) [15]		
24 h	2 OR 0.78 (0.17; 3.55) [23] OR 1.17 (0.91; 1.50) [17]	2 OR 0.36 (0.13; 0.98) [19] OR 0.53 (0.29; 0.99) [24]	
Discharge	2 OR 1.09 (0.46; 2.60) [18] OR 1.14 (0.40; 3.20) [25]	2 OR 0.65 (0.55; 0.78) [8] OR 0.44 (0.27; 0.71) [20]	
3 days	1 OR 1.18 (0.38; 3.63) [10]	2 OR 0.45 (0.27; 0.76) [9] OR 0.24 (0.10; 0.57) [31]	
1 week	1 OR 0.78 (0.17; 3.55) [23]		
20 days	1 OR 0.72 (0.26; 1.98) [19]		
4 weeks	2 OR 1.48 (0.54; 4.08) [15] OR 0.86 (0.14; 5.27) [23]	1 OR 0.59 (0.44; 0.80) [31] aOR 1.26 (1.10; 1.44) [31]	
6 weeks	1 OR 1.45 (0.87; 2.40) [20] aOR 0.75 (0.41; 1.38) [20]	1 OR 0.57 (0.41; 0.78) [9]	1 OR 2.39 (1.36; 4.19) [10]
8 weeks		1 OR 0.63 (0.46; 0.88) [7]	

aOR- adjusted Odds ratio.

**Fig. 2.** Forest plot presenting Odds ratios and 95% Confidence Intervals (95% CI) of studies assessing breastfeeding success at 2 to 8 weeks postpartum.

Ding et al. found no significant difference between groups (OR 1.18 (95%CI, 0.38; 3.63)) [10].

Mahomed et al. measured breastfeeding at discharge and found a significantly lower incidence of breastfeeding in the NA group, OR 0.44 (95%CI, 0.27; 0.71). [20]

Mauri et al. assessed breastfeeding at 20 days and found no difference between groups, OR 0.61 (95%CI, 0.15; 2.44). [19]

Three studies measured breastfeeding at 6 weeks using a dichotomous outcome. Of these studies, two found no statistically significant difference between the NA and control group (OR 0.73 (95% CI, 0.46; 1.17)) [20], OR 0.61 (95%CI, 0.32; 1.16)) [9]. In contrast, Ding et al. found a significantly higher breastfeeding rate in the NA group compared to the control group, OR 2.39 (95%CI, 1.36; 4.19). [10]

Henderson et al. measured at 2 months postpartum and found a significantly lower breastfeeding rate in the NA group, OR 0.63 (95%CI, 0.46; 0.88). [7]

Analysis excluding studies with a serious and critical risk of bias.

Looking only at low and moderate risk of bias studies in mixed-parity cohorts we found the following results.

At 3 h, Wilson et al. found no significant difference in breastfeeding rates, OR 1.02 (95%CI, 0.80; 1.30). [17]

At 24 to 48 h, Wilson et al. found no significant difference (OR 1.17 (95%CI, 0.91; 1.50)) [17], whereas Mauri et al. did (OR 0.36 (0.95%CI, 0.13; 0.98)) [19].

At discharge, Wetzl et al. found a significantly lower incidence of breastfeeding in the NA group, OR 0.65 (95%CI, 0.55; 0.78). [8]

At 3 days, Orbach-Zinger et al. found a significantly lower incidence of breastfeeding, OR 0.45 (95%CI, 0.27; 0.76). [9]

At 20 days, Mauri et al. found no significant difference, OR 0.72 (95%CI, 0.26; 1.98). [19]

At 6 weeks, Orbach-Zinger found a significantly lower incidence of

breastfeeding, OR 0.57 (95%CI, 0.41; 0.78). [9]

At 8 weeks, Henderson et al. found a significantly lower incidence of breastfeeding rates, OR 0.63 (95%CI, 0.46; 0.88). [7]

4. Discussion

In this systematic review we compared breastfeeding success between parturients that received NA and those that did not (non-NA/no analgesia). We quantified all of the data given in the individual articles by calculating ORs and 95% CI in order to test for statistical significance.

Overall, there were 6 studies that found no difference between groups, 6 studies that showed a significantly lower incidence of breastfeeding in the NA group and 3 studies with mixed results (i.e. one study found a statistically significant result at one time-point, but a statistically non-significant result at another time-point).

In the nulliparous only studies, 2 found no difference between study groups, 1 found a lower breastfeeding rate in the NA group and 3 studies showed mixed results.

When excluding studies with critical and high risk of bias, 1 study found no difference between study groups, 3 studies found a decrease of breastfeeding rates in the NA group, and 1 study showed mixed results.

There are many possible reasons for the discrepancy found between studies. First, there are no randomized controlled trials comparing NA and non-NA on the incidence of breastfeeding and thus women themselves choose whether to receive NA or not. Women electing to undergo childbirth without NA may have been more inclined to breastfeed. Also, a woman's choice of NA may also have reflected a longer and more difficult labor. Often, NA is chosen in very exhausting and difficult labors after which parturients may be very tired and thus choose to delay onset of breastfeeding. [21] Furthermore, breastfeeding success is determined by many influences including pre-pregnancy, intrapartum, and postpartum factors. Many studies have not controlled for important confounders including previous breastfeeding experience [22–24], immediate skin to skin placement [7,10,15] or lactation-friendly hospitals [8,17] or maternity-leave after labor. [18,20,25] Furthermore, there is no consistency in breastfeeding education and support available in all hospitals. [26,27]

In addition, the discrepancy can be explained by geographic differences. Studies were performed in United Kingdom, Iran, Australia, Israel, USA, Canada, Italy, Spain, China. Each country has different breastfeeding norms and different postpartum rituals that may affect breastfeeding incidence.

Previous studies have suggested that epidural fentanyl may have a role in decreased breastfeeding success via decreased neurobehavioral infant scores. [28] We were unable to conduct a subgroup analysis for this factor because most studies used fentanyl, but did not show the amount of fentanyl administered. A recent study by Lee et al. showed that epidural fentanyl < 150 µg is not a factor in breastfeeding success. [29]

The strengths of our systematic review are the different time-points analyzed, the meticulous examination of risk of bias, the conduction of a subgroup analysis and the quantification of the results of individual studies.

The limitations include possibility of having missed an article in our literature searches when the term breastfeeding was not mentioned in the title or abstract of a study. By using multiple search engines and hand-searching the references, we tried to decrease the chance of missing an article. The second limitation is the heterogeneity in the quality of the studies. Furthermore, there is a risk of uncontrolled and possible unreported confounding when dealing with observational studies. We were unable to do a subgroup-analysis of multiparous-only women because there were not enough data available.

Epidural analgesia is a very popular and effective technique to provide labor analgesia. [6,30] Thus, it is very unlikely that randomized controlled trials that compare epidural analgesia with no

analgesia or opioid analgesia with the outcome breastfeeding will be performed.

In conclusion, we found a high heterogeneity in study results and study-designs. The included studies with a mainly observational study design carry the risk of confounding, by either known or unknown factors, that make it impossible to conclude causality between neuraxial analgesia and breastfeeding success. Observational studies only allow conclusions about possible associations. Breastfeeding success is influenced by many factors and neuraxial labor analgesia most likely only plays a small, if any, role in this complex relationship. We believe that neuraxial analgesia for labor should not be avoided out of fear of a strong impact on continued breastfeeding success.

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CRediT authorship contribution statement

Philip Heesen: Conceptualization, Data curation, Writing - original draft, Writing - review & editing. **Stephen H. Halpern:** Conceptualization, Methodology. **Yaakov Beilin:** Conceptualization, Writing - original draft. **Paola A. Mauri:** Formal analysis. **Leonid A. Eidelman:** Conceptualization. **Michael Heesen:** Conceptualization, Methodology. **Sharon Orbach-Zinger:** Conceptualization, Data curation, Writing - original draft.

Declaration of Competing Interest

None.

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